REMARKS

Applicant respectfully requests reconsideration. Claims 19, 21, 25-27, and 29-35 were previously pending in this application. By this amendment, Applicant is canceling claims 30-35 without prejudice or disclaimer. Claims 19, 21, 25-27, 29, and 30 have been amended. New claims 36-48 have been added. Support for the claim amendments and the new claims can be found in the specification at least on page 5, lines 6-12; page 6, lines 4-14; page 9, line 17, through page 11, line 26; and Figs. 1 and 2. As a result, claims 19, 21, 25-27, 29, 30, and 36-48 are pending for examination with claims 19, 38, and 47 being independent claims.

No new matter has been added.

Rejection under 35 U.S.C. §112, first paragraph

The Examiner rejected claims 19, 21, 25-27, 29, and 30 under 35 U.S.C. §112, first paragraph, for an alleged lack of enablement. According to the Examiner, the specification does not reasonably provide enablement for 1) a DNA construct for providing a heterologous immunoglobulin in the milk of a non-human mammal that lack operable linkage between the promoter and the coding sequence for the immunoglobulin and 2) a DNA construct encoding both heavy and light chain immunoglobulin genes that comprise two different mammary specific promoters.

Applicant respectfully disagrees. First, in the interest of expediting prosecution of the instant application and without conceding the correctness of this rejection, Applicant has amended the rejected claims such that the claims recite that the promoter sequences are operably linked.

Second, based on the teachings provided in the instant specification and the level of skill of those of ordinary skill in the art, Applicant maintains that the claims are enabled for the expression of immunoglobulin sequences using the same or different mammary specific promoters. The specification provides a variety of mammary specific promoters, such as caseins promoters, lactalbumin promoters, and whey acid promoters that can be used to express proteins in the mammary gland (See *e.g.,* page 6, lines 4-14 of the specification). The specification further teaches how to use the promoters in combination with the heterologous immunoglobulin sequences to be expressed (See *e.g.,* page 10, line 26 through page 11, line 21) and how to determine the expression

level of a protein that is operably linked to a promoter (See *e.g.,* page 12, line 28 through page 13, line 24).

Based on at least these teachings, one of ordinary skill would be able to determine which promoters would provide for an appropriate expression level of the heavy and light chains of an immunoglobulin, and the Examiner has not demonstrated otherwise. The Examiner merely argues that the heavy and light chains cannot be expressed by different promoters because the use of two different milk specific promoters would not predictably result in the concomitant expression of the light and heavy chains at the appropriate levels. Such a conclusory argument is not sufficient to maintain this rejection. The Examiner has not met her burden in establishing that undue experimentation would be required for one of ordinary skill in the art to make and use the DNA constructs and cells of the claims. Applicant maintains that with the teachings provided and the level of skill of those of ordinary skill in the art, undue experimentation would not be required to practice the claimed invention. The claims, therefore, are enabled.

Accordingly, reconsideration and withdrawal of this rejection is respectfully requested.

Rejection under 35 U.S.C. §112, second paragraph

The Examiner rejected claims 19, 21, 25-27, 29, and 30 under 35 U.S.C. §112, second paragraph, for allegedly being indefinite.

According to the Examiner, the phrase "primarily…of human origin" in claim 19 is indefinite. Without conceding the correctness of the Examiner's rejection, and in the interest of expediting prosecution, Applicant has amended claim 19 such that the rejected phrase no longer appears.

According to the Examiner, the phrase "wherein each coding region" in claim 19 is indefinite. Without conceding the correctness of the Examiner's rejection, and in the interest of expediting prosecution, Applicant has amended claim 19 and deleted the rejected phrase such that it no longer appears.

According to the Examiner, the phrase "wherein each coding region may be expressed individually" in claim 19 is indefinite. Without conceding the correctness of the Examiner's

rejection, and in the interest of expediting prosecution, Applicant has amended claim 19 such that the rejected phrase no longer appears.

According to the Examiner, the phrase "wherein the immunoglobulin protein coding sequence encodes a heavy chain coding region; wherein said immunoglobulin protein coding sequence encodes a light chain coding region" in claim 19 is indefinite. Without conceding the correctness of the Examiner's rejection, and in the interest of expediting prosecution, Applicant has amended claim 19 such that it is believed that the Examiner's rejection is moot.

According to the Examiner, the phrase "A mammary epithelial cell comprising the construct of claim 19 and a construct comprising an immunoglobulin protein coding sequence which encodes both a light and heavy chain operatively linked to a promoter..." is indefinite. Without conceding the correctness of the Examiner's rejection, and in the interest of expediting prosecution, Applicant has amended claim 29 such that it is believed that the Examiner's rejection is moot.

In light of the above, reconsideration and withdrawal of this rejection is respectfully requested.

Rejection Under 35 U.S.C. §103

The Examiner rejected claims 19, 21, 25-27, 29, and 30 under 35 U.S.C. §103(a) as allegedly being unpatentable over Surani (WO 90/04036), De Boer (US 5,633,076), Meade (US 4,873,316), Bischoff (FEBS Letters 305:265-268, 1989), Buhler (Bio/Technology 9:835-838, 1991) Gordon et al. (Bio/Technology 5:1183-1187, 1987), Ebert (Bio/Technology 8:140-143, 1990), and Stinnakre (FEBS letters 284: 19-22, 1991). According to the Examiner, Surani et al. teach a construct for providing an Ig to serum of a transgenic mouse. Further, according to the Examiner, Surani et al. teach that such constructs can be modified by means known in the art to target the expression of said nucleic acids encoding the heavy chain and light chain to milk of transgenic animals. Also, according to the Examiner, Surani et al. do not teach a promoter that results in the expression of the Ig coding sequence in mammary epithelial cells and milk. However, according to the Examiner, DeBoer et al. teach an expression construct for expressing a heterologous protein, most preferably a lactoferrin protein, into the milk of cows. In addition, according to the Examiner,

Meade et al., Gordon et al., Ebert et al., and Stinnakre et al. teach constructs including the claimed promoters for the expression of proteins in the mammary gland.

Applicant respectfully traverses. The cited references do not teach or make obvious the constructs and cells of the claims. One of ordinary skill in the art would not have had a reasonable expectation of success in using the constructs and cells of the claims. Therefore, one of ordinary skill in the art would not have been led to create, and in fact would have been discouraged from creating, the claimed constructs and cells.

Without the teachings in the instant application, one of ordinary skill in the art would not have expected that functional, assembled immunoglobulin could be produced with constructs encoding both the heavy and light chains of an immunoglobulin or with cells that express both the heavy and light chains in the same cell. In fact, without the teachings provided, one of ordinary skill in the art would not have had a reasonable expectation of success in producing functional, assembled immunoglobulin with the claimed constructs and cells because of factors that included 1) the variety of co- and post-translational modifications that nascent immunoglobulin polypeptides undergo; 2) the availability of accessory proteins for the assembly of immunoglobulins; and 3) the stability of expressed recombinant immunoglobulins in the extracellular milieu of a foreign cell, etc. Accordingly, the Examiner has not been sufficiently demonstrated that one of ordinary skill in the art would have had a reasonable expectation of success in using the constructs and cells of the claims based on the teachings of the cited references. Therefore, one of ordinary skill in the art would not have been led to created the claimed constructs and cells, and the claimed constructs and cells are not obvious.

Accordingly, reconsideration and withdrawal of this rejection is respectfully requested.

CONCLUSION

A Notice of Allowance is respectfully requested. The Examiner is requested to call the undersigned at the telephone number listed below if this communication does not place the case in condition for allowance.

If this response is not considered timely filed and if a request for an extension of time is otherwise absent, Applicant hereby requests any necessary extension of time. If there is a fee occasioned by this response, including an extension fee, the Director is hereby authorized to charge any deficiency or credit any overpayment in the fees filed, asserted to be filed or which should have been filed herewith to our Deposit Account No. 23/2825, under Docket No. G0744.70014US02.

Dated: December 1, 2009

Respectfully submitted,

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